II. Remarks

Claims 1, 2, 4, 5, 7-12 and 39-52 are pending. Claim 53 has been cancelled without prejudice.

New Rejections

A. Rejection under 35 U.S.C. § 112

In the Office Action, the Examiner rejected new claim 53 under 35 U.S.C. § 112, first and second paragraphs as failing to comply with the written description requirement and as being indefinite.

Applicants respectfully traverse these rejections. Claim 53 has been cancelled without prejudice. Accordingly, the Examiner's rejections are moot. In view of the above-noted claim cancellation, Applicants respectfully request that the Examiner's 112 rejections be removed.

Maintained Rejections

A. Rejection under 35 U.S.C. §103

In the Office Action, the Examiner maintained the rejections of claims 1-2, 7-12, 39-40 and 45-50 and new claim 53 under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 4,910,023 to Botzolakis et al. ("Botzolakis"). At page 6 of the office action the Examiner stated that:

> "It would have been obvious…to use the method of making a tablet comprising drying a slurry containing a moisture sensitive ingredient, colloidal silicon dioxide and microcrystalline cellulose, as suggested by Botzalakis, vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline cellulose

> during the process of routine optimization, and produce the instant invention. One of ordinary skill in the art would do this because during the process of routine experimentation the step of drying the microcrystalline cellulose and colloidal silicone dioxide in the drug slurry can be varied to adding the drug to the dried microcrystalline cellulose and colloidal silicon dioxide slurry. One with ordinary skill in the art would change the addition of drug the dried microcrystalline cellulose and silicon dioxide mixture in order to optimize the taste masking and desired release profile of the drug."

Applicants respectfully disagree with the Examiner's assertions. Both independent claims 1 and 39 of the present invention claim a process for preparing a tablet formulation wherein the active ingredient is combined with a novel excipient. Prior to tableting with the active ingredient, the excipient is prepared by forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide and drying the slurry to obtain an excipient (claim 1); or by preparing separate aqueous slurries of the microcrystalline cellulose and silicon dioxide and introducing these slurries separately into a drying apparatus to obtain an excipient (claim 39). In both of these claimed processes, the microcrystalline cellulose/silicon dioxide excipient is first dried before being combined with the active ingredient.

In contrast, the "unique" wet granulation process described in the Botzalakis reference does not, as admitted by the Examiner, "expressly teach drying a slurry of microcrystalline cellulose and silicon dioxide before mixing with a moisture-sensitive active ingredient."

Furthermore, it would not have been obvious to one of ordinary skill in the art reading the disclosure of the Botzalakis reference to "vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline cellulose during the process of routine optimization", nor would one of ordinary skill in the art have considered "varying the addition of drug to a dried microcrystalline cellulose and silicon dioxide mixture" as suggested by the Examiner. In fact, based on the disclosure of the Botzalakis reference, one of skill in the art would understand that the Botzalakis reference teaches away from the present invention because the "unique" wet granulation process described therein requires all

ingredients, to be mixed via wet granulation and then dried. For example, the Examiner is directed to Examples 1 and 2 of the Botzalakis reference. In Example 1, drug is first milled with colloidal silicon dioxide (SiO_2) and screened. Next an aqueous mixture of sodium lauryl sulfate is mixed with the drug/SiO_2 mixture. Additional SiO_2 is added followed by the addition of microcrystalline cellulose. The final granulation is then dried. (See: Botzalakis, col. 3) Similarly, in Example 2, drug is dissolved in water, colloidal silicon dioxide is added and mixed, and microcrystalline cellulose is subsequently added and mixed. The final granulation is then dried. (See: Botzalakis, col. 4). Thus, in view of the explicit teaching in the Botzolakis reference of the "unique" wet granulation process, one of skill in the art would not have attempted to "change the addition of drug to the dried microcrystalline cellulose and silicon dioxide mixture in order to optimize the taste masking and desired release profile of the drug" as suggested by the Examiner.

Moreover, unlike the present invention wherein the excipient is dried to form a pre-manufactured excipient, the "unique" wet granulation process described in the Botzalakis reference teaches away from a process wherein the excipient is a dried, pre-manufactured excipient.

In view of the above arguments, Applicants respectfully submit that independent claims 1 and 39 are not obvious over the Botzalakis reference. Therefore, Applicants respectfully request that the Examiner's rejection be removed. Since claims 1-39 are not obvious over the teachings of the Botzalakis reference, dependent claims 2, 4, 5, 7-12 and 39-52 are also not obvious over the Botzalakis reference. Accordingly, the Examiner's obviousness rejection in view of these dependent claims should also be removed.

In the Office Action, the Examiner also maintained the rejection of claims 4-5, 41-44 and 51-52 under 35 U.S.C. §103(a) as being unpatentable over Botzolakis in view of United States Patent No. 4,605,666 to Schmidt et al. ("Schmidt"). The Examiner stated "Botzolakis does not expressly teach spray drying." The Schmidt reference is being relied upon for teaching "a process for preparing a powder … which is directly compressible into a tablet prepared by spray drying (a) an aqueous slurry of a water-soluble vitamin and a binder, (b) … an adsorbent and (c) a lubricant (Abstract)." The Examiner then asserted "it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of making a tablet … as taught by Botzolakis, vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline cellulose during the process of routine optimization, combine it with the process of spray drying to produce a compressible powder, and produce the instant invention."

The Examiner's rejection is respectfully traversed. Applicant reasserts the arguments presented above in connection with the Botzolakis reference. The deficiencies of Botzolakis are not cured by Schmidt. Schmidt describes a process where a water soluble vitamin is prepared into an aqueous slurry with microcrystalline cellulose that is spray-dried and silicon dioxide and magnesium stearate added to the drying chamber. Both Botzolakis and Schmidt fail to provide a basis for a person having ordinary skill in the art at the time of the invention to form a "pre-manufactured" excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which advantageously protects the moisture-sensitive active, as provided by the subject invention. Accordingly, claims 4-5, 41-44 and 51-52 are not obvious over the Botzalakis reference in further view of the Schmidt reference. Therefore, Applicants respectfully submit that the Examiner's rejection be removed.

B. Obviousness-type Double Patenting Rejection

In the instant Office Action the Examiner maintained the nonstatutory obviousness-type double patenting rejections in view of U.S. Patent Nos. 6,103,219; 6,746,693. These rejections were maintained because the terminal disclaimers were signed by an attorney not listed on the Power of Attorney.

In response, Applicants have submitted new terminal disclaimers signed by Leslye B. Davidson, who is listed on the Power of Attorney. Applicants believe the submission of these terminal disclaimers obviates all outstanding obviousness-type double-patenting rejections, and respectfully request approval of the terminal disclaimers and withdrawal of these rejections.

III. Conclusion

In view of the arguments presented, it is respectfully submitted that the present application is now in condition for allowance. An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy, the Examiner is specifically authorized to contact the undersigned in the event that a telephonic interview will advance the prosecution of the application. A request for a one-month extension of time to reply to the Office Action along with an authorization for the Commissioner to charge the undersigned's Attorney Deposit Account the requisite fees is also submitted herewith. It is believed that no additional fees are due for this submission. If it is determined that additional fees are due or that any fee has been overpaid, the Commissioner is hereby authorized t charge said fees or credit any overpayment to Deposit Account No. 50-0552.

Respectfully submitted,
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